MBL

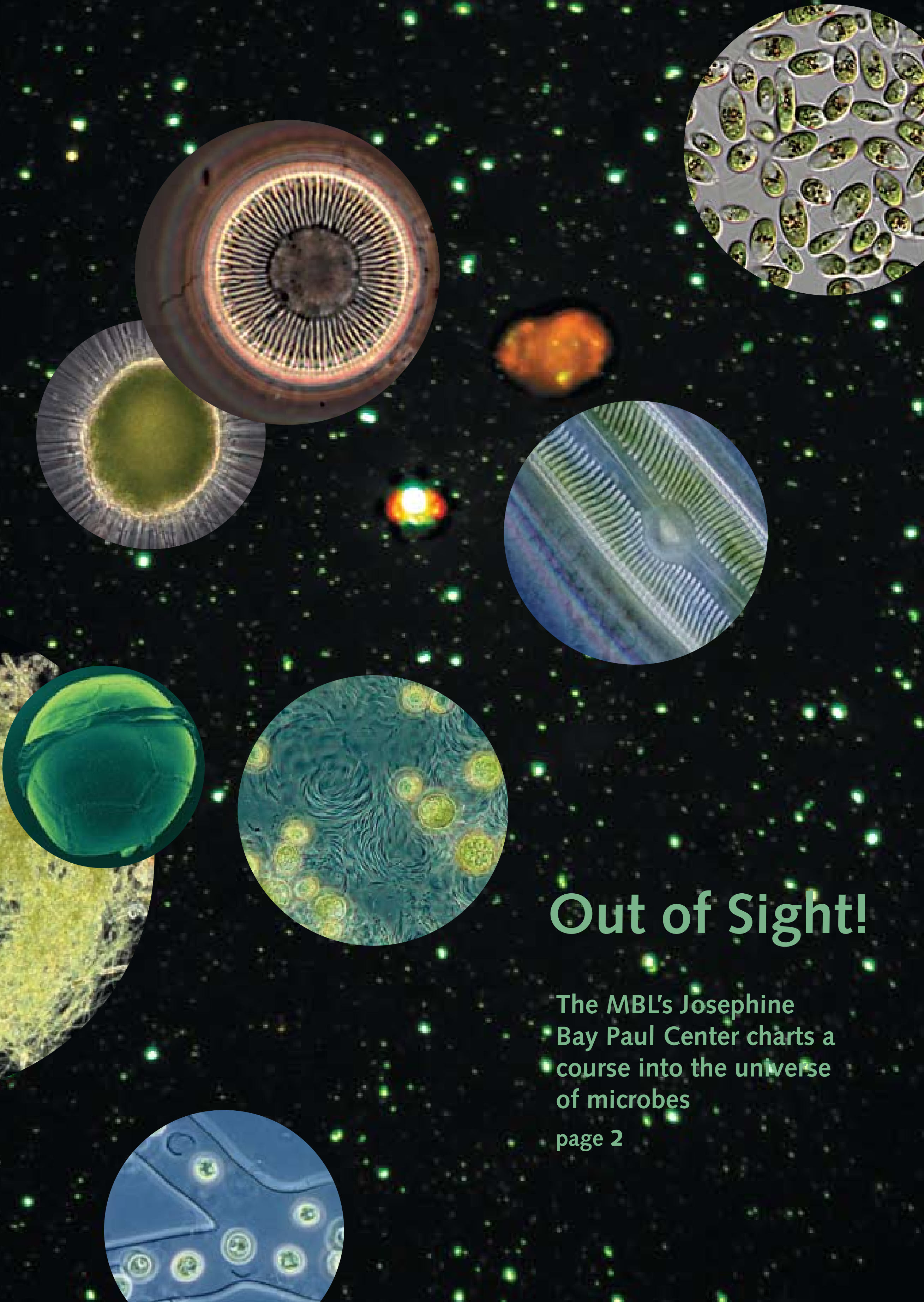
Catalyst

Biological Discovery in Woods Hole

Founded in 1888 as the Marine Biological Laboratory

Fall 2007
Volume 2, Number 2

IN THIS ISSUE



Out of Sight!

The MBL's Josephine Bay Paul Center charts a course into the universe of microbes

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MBL Catalyst

Fall 2007 Volume 2, Number 2

MBL Catalyst is published twice yearly by the Office of Communications at the MBL in Woods Hole, Massachusetts. The MBL is an international, independent, nonprofit institution dedicated to discovery and to improving the human condition through creative research in the biological, biomedical, and environmental sciences. Founded in 1888 as the Marine Biological Laboratory, the MBL is the oldest private marine laboratory in the Western Hemisphere.

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About the cover: Background image by J. Furhman: Marine microbes are so plentiful, they resemble the stars in the night sky. Floating microbes by D. Patterson, provided by micro*scope: http://microscope.mbl.edu, copyright MBL.

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From the Editor

Dear Friends,

My family is thinking a lot about microbes these days. In December, we are leaving the Cape for a two-week safari in East Africa. It's a trip of a lifetime, but one that requires some preparation if we're to protect ourselves from disease-causing organisms we cannot see.

We've had this vaccine and that to ward off microbes like Flavivirus, *which causes the deadly yellow fever. We've been warned against drinking local water and eating certain fruits and vegetables to avoid contracting pathogens like* Giardia. *At a recent dinner party, one colleague even cautioned against stepping in water holes to guard against the parasitic flatworm that causes schistosomiasis, an infection, he also told me, that is at least treatable.*

We will arrive in Africa armed with Cipro, just in case our efforts to avoid various forms of food poisoning, like typhoid, fail. And we will faithfully take our Malarone throughout our trip to ward off malaria, a disease that sickens and kills more children in Africa than any other.

But pathogenic microbes aren't simply a concern of the Third World. Infectious microbes live everywhere that humans live, evolving alongside us, often keeping a step or two ahead of us. Just this week, for example, public schools in Massachusetts were taking precautionary measures against MRSA, a drug-resistant form of Staphylococcus *bacteria that can cause deadly infections.*

But all this talk of disease gives microbes a bad name. As you'll see in this issue of MBL Catalyst, *microbes of all kinds are essential to our very survival. They are key players in the indispensable cycles that keep Earth habitable, from photosynthesis to decomposition, and they have developed countless strategies for adapting to a changeable world. Microbes have a lot to teach us, with implications ranging from climate change research to drug development. And, as this issue shows, the MBL is at the forefront of exploring the tremendous potential of microbes.*

Many thanks to Mitch Sogin, director of the Josephine Bay Paul Center, for serving as our guest editor for this issue. An intrepid explorer of the microbial world, Mitch is also a thoughtful and precise editor. I am most grateful for his efforts. I'd also like to introduce Diana Kenney, an alumna of the MBL's Science Journalism Program and our new staff science writer, who wrote the majority of the articles in this issue.

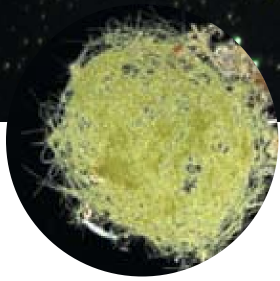
As you read through the pages of Catalyst, *I hope you'll enjoy exploring the microbial world as much as our scientists and students do. As always, your comments are most welcome.*

Pam Hinkle

Pamela Clapp Hinkle
Editor-in-Chief
Director of Communications

Catalyst

In this Issue



MBL

Out of Sight!

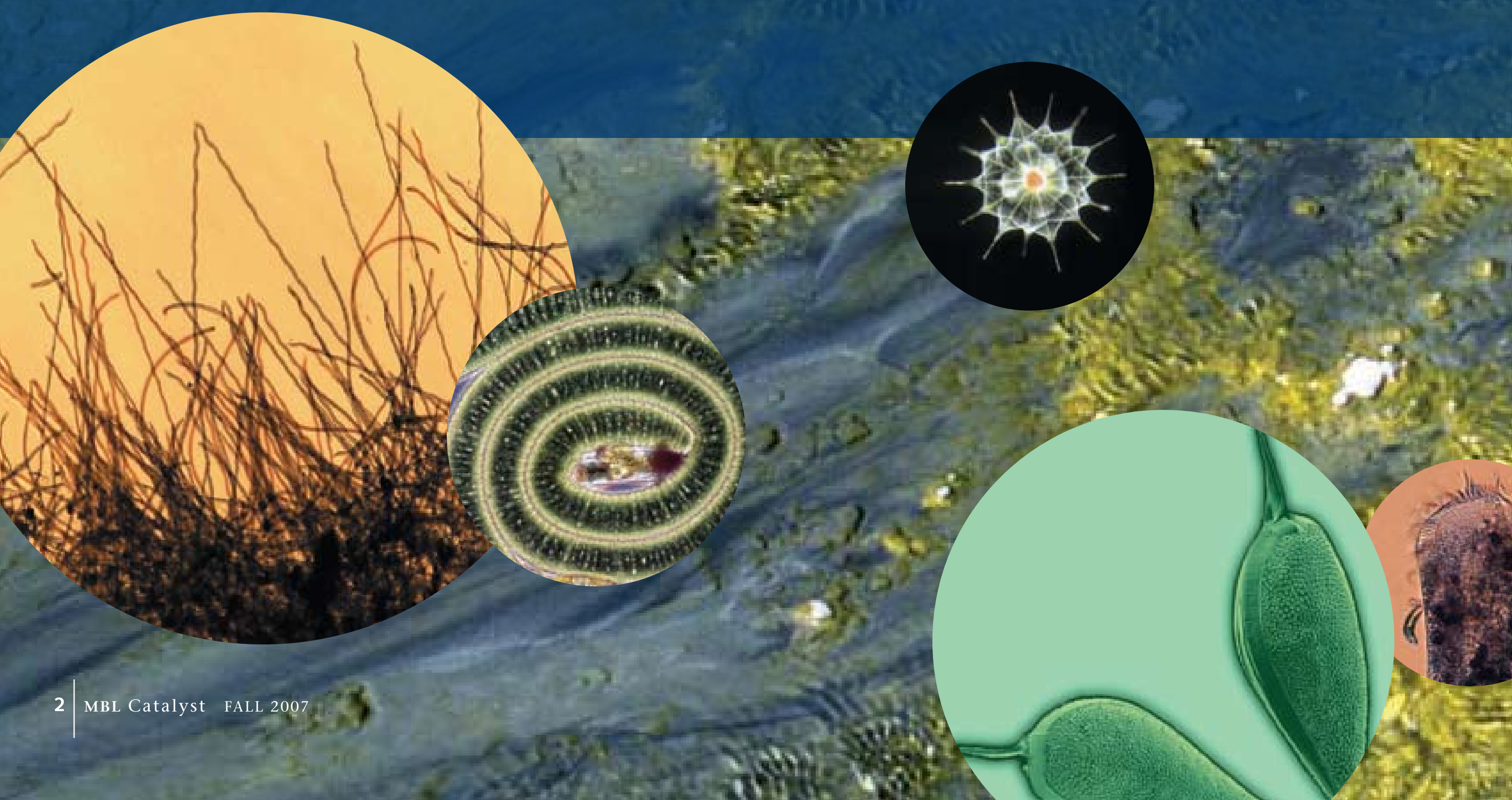
The Josephine Bay Paul Center is a world leader in exploring the universe of microbes

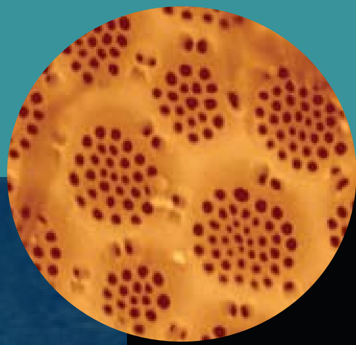
When it comes to microbes, small is big. Very big.

Microbes were the first life to appear on Earth, more than three billion years before humans emerged. Amazingly numerous and diverse, they live everywhere on the planet. Some survive extreme heat, pressure, or toxicity; some need only vanishing amounts of energy to grow. Were there to be a cataclysmic event on Earth, microbes would begin the web of life again.

Indeed, without microbes, life would stop. Microbes produce most of our oxygen and process carbon and nitrogen—all key elements of life. They provide plants and animals with vital nutrients and vitamins. In our bodies, microbes digest food and protect us from disease. Some, the pathogens, make us sick.

Despite our dependence on these microscopic creatures, they remain mysterious. Of the estimated millions of microbial species, less than one-tenth of one percent have been described. At the MBL's Josephine Bay Paul Center (JBPC), scientists are making leaps in discovering what microbes are out there, their role in maintaining the biosphere, and how they evolve.





Scientists at the JBPC cast a wide net, studying microbes in ecosystems across the globe—from ocean bacteria that affect human health, to soil microbes that factor into climate change, to the "extreme," resilient species that might resemble life forms on distant planets. Using imaginative, massively parallel, high-throughput DNA sequencing strategies, the JBPC is making some of the world's first global maps of microbial diversity.

The universe of microbes is vast, varied, and still largely undiscovered. At the JBPC, scientists are eager to explore it.

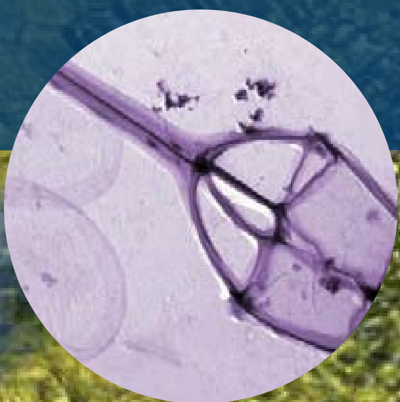
What is a microbe?

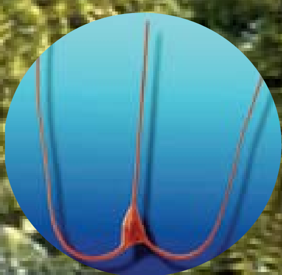
- Microbes are microscopic organisms from three kingdoms of life: Bacteria, Archaea, and Eukarya.

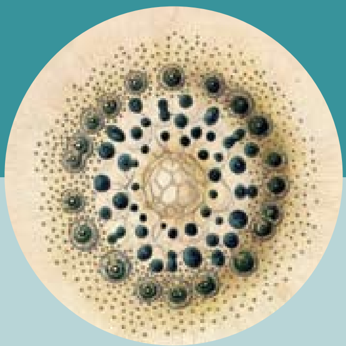
- Eukaryotic cells have a nucleus and an elaborate cytoskeleton, or cell framework. Bacterial and archaeal cells lack these features.

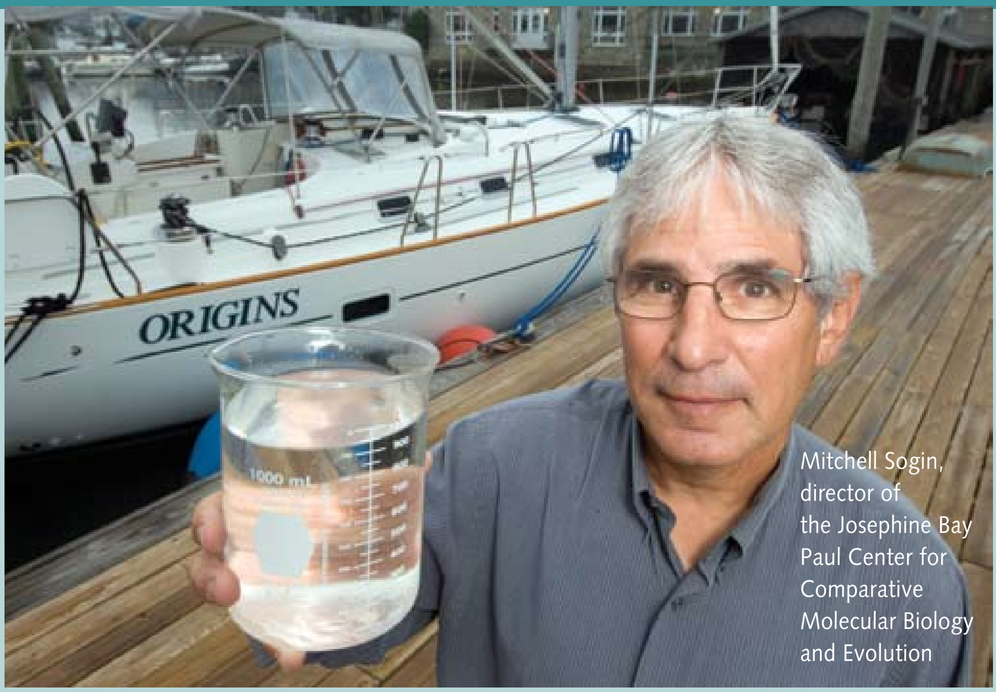
- Scientists traditionally classified microbes by morphological and cell staining characteristics, metabolism, or by the chemical reactions they perform. For example, the methanogens are archaea that produce methane gas; the cyanobacteria are bacteria that perform photosynthesis. Today, the application of modern DNA technology has led to a new understanding of how microbes are related to each other and how their properties have evolved.

- Over the past two decades, the number of known microbial phyla has soared from 12 to 120. "And this is just scratching the surface of the major lineages of microbes," says Mitchell Sogin, director of the JBPC.









Mitchell Sogin, director of the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution

There are **10,000,000,000,000,000,000,000,000,000** *microbial cells in the ocean.*

Talk about making a splash! When Mitchell Sogin and his colleagues set out to estimate how many kinds of bacteria the ocean holds, they expected to find a few thousand. Astonishingly, the more they looked, the more they found—"and the species discovery curve is still going to the moon," says Sogin, director of the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution.

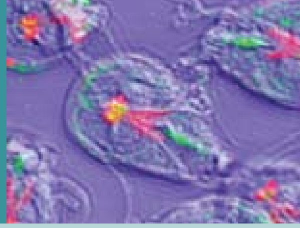
Sogin's team found more than 38,000 kinds of bacteria in one liter of seawater—and that's not to say different scoops of ocean wouldn't contain thousands, even millions of other microbial novelties. Their startling discovery made headlines around the world.

For Sogin, just as striking as the sheer number of microbial types found in the ocean is their relative abundance. The study, which is part of the International Census of Marine Microbes (ICoMM), found a few dominant, fast-growing species of bacteria in the samples tested. But beyond these "more common" species lay thousands of species whose populations are tiny in comparison. This "rare biosphere" of low-abundance organisms is a whole new level of marine life to explore.

In the next phase of the ICoMM, Sogin and his colleagues are analyzing 1,200 ocean samples from around the world, from different depths and environments. "Understanding the basic population structure of the microbes is the first step," says JBPC assistant scientist Julie Huber. "Who are the dominant players, who are the rare members, and what might their roles be? In some parts of the ocean, particularly the photosynthetic upper water column, we already understand a lot. But in the deep sea, we know much less. It really is an unexplored frontier."

New Maps into New Worlds

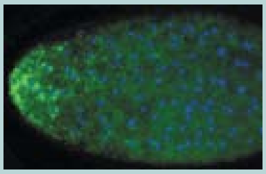
Uncharted waters call for the best navigational tools, and Sogin has developed a powerful way to detect the different kinds of microbes in an environmental sample and their relative abundance. Using what he calls "454 tag sequencing," Sogin sorts organisms by how they vary in a tiny region of the same gene. Although it was invented for the ICoMM, tag sequencing has broad applications. One new study uses it to assess the diversity of bacteria living in soil, including microbes that contribute to the flux of greenhouse gases. Another initiative will inventory changes in the microbial populations found in the digestive track of mammals, including humans, where more than 4,000 different kinds of microbes live. And the



microbes that populate a Cape Cod swimming area and nearby marsh are the focus of a third tag sequencing study. One day, health officials may rely on this technology to target the sources of contamination at popular beaches.

Microbes and Evolution

"We are in the heyday of appreciating how important microbes are to evolutionary change and to our own existence," says JBPC assistant scientist Seth Bordenstein.



Given their variety, microbes are a potent reservoir for genetic diversity on Earth—a kind of safe deposit against threats to mass extinction. They are also the busy agents of evolutionary change, freely exchanging genetic information sexually or through lateral transfer. Bordenstein and JBPC associate scientist Jennifer Wernegreen zero in on the "co-dependent" bacteria, the endosymbionts, which are engulfed by and live inside the very tissues or cells of their hosts. These intimate microbe-host associations have prompted major evolutionary and ecological transitions, including the rise of the eukaryotic cell and the emergence of new insect species. Other JBPC investigators hope to pin down mobile DNA—genes that jump around in the genome—long enough to discover its roles in microbial evolution.

The Wide World of the Very Small

The universe itself is the limit of inquiry into microbes at the MBL, and this issue of *Catalyst* traverses habitats from the ocean depths to Mars and back home again. As a lead team in NASA's Astrobiology Institute, the JBPC embraces the search for life on other planets. And the spectacular array of microbial diversity on Earth is of no less interest. The MBL is a cornerstone institution in the epic-scale Encyclopedia of Life project, which plans to create a Web page for each of the Earth's 1.8 million named species, plus the countless more that await discovery, including microbes. And, if history repeats itself, some of those microbes will be discovered by students in the MBL's Microbial

Diversity course, right here in the ponds, marshes and bays of Woods Hole (see story on page 10). •

Josephine Bay Paul Center

Researchers at the Josephine Bay Paul Center investigate the genomes of diverse organisms that play significant roles in environmental biology and human health. Current sponsored projects include:

W.M. Keck Foundation
- W.M. Keck Ecological and Evolutionary Genetics Facility

National Institutes of Health
- Evolution and gene expression in the human parasites *Giardia* and *Schistosoma*
- Influence of endosymbiotic relationships on bacterial genome evolution
- Relationships between eukaryotes through comparisons of expressed genes
- Marine-related studies of human health in collaboration with the Woods Hole Center for Oceans and Human Health (also funded by the National Science Foundation)

National Science Foundation
- Molecular evolution of endosymbionts
- Genomics of terrestrial microbial communities associated with the production and consumption of greenhouse gases
- Development of digital resources for describing microbial diversity
- Molecular evolution studies of rotifer and microsporidial genomes
- Microbial inventory research across diverse aquatic LTERS

Alfred P. Sloan Foundation
- International Census of Marine Microbes
- Visual analysis of microbial populations
- Combinatorial imaging and metagenomics of microbial communities

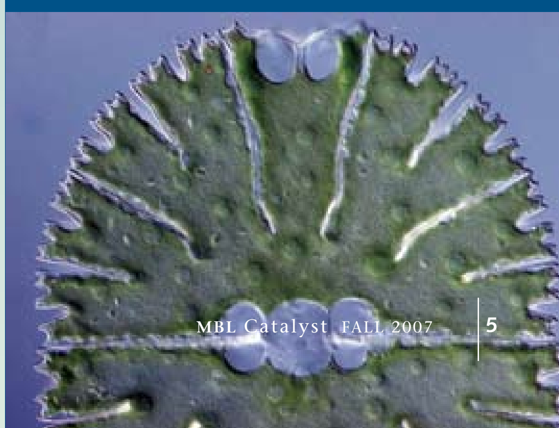
National Aeronautics & Space Administration
- MBL Astrobiology

Howard Hughes Medical Institute
- Discover the Microbes Within

U.S. Department of Energy
- Annotation and evolution of gene families in *Shewanella oneidensis*

Educational Programs

The JBPC accepts students in the Brown-MBL Graduate Program in Biological and Environmental Sciences. JBPC scientists also teach in the MBL's Parasitology course, Microbial Diversity course, and the renowned Workshop on Molecular Evolution. Two workshops for secondary school teachers are offered annually: Living in the Microbial World and Discover the Microbes Within.



Exploring New Orleans' Post-Hurricane Microbial Landscape

Years after Hurricanes Katrina and Rita slammed into New Orleans, sediments in the city remain contaminated with fecal microbes, and water quality in the city and in nearshore waters of Lake Pontchartrain continues to be impacted by this contamination. MBL associate research scientist Linda Amaral Zettler and her colleagues reported these results in a study published this year in the *Proceedings of the National Academy of Sciences* which documented the microbial landscape of the region following the hurricanes. Using DNA sequencing technology, the MBL led the multi-institutional effort to analyze overall microbial diversity in water and sediment samples taken from the canals and shoreline of New Orleans and the offshore waters of Lake Pontchartrain after floodwaters had receded. This provided a big-picture view of the kinds of microbes in the environment and whether they were similar in makeup to known pathogens or to microbes typically found in sewage treatment. Results of the study indicated that while floodwaters pumped from New Orleans back into Lake Pontchartrain following the hurricanes showed higher-than-normal levels of bacteria and pathogens, fecal indicator microbe and pathogen concentrations in the lake returned to pre-hurricane levels within two months. However, the sediments left behind in the flooded regions of the city appear to contain microbes commonly found in sewage treatment and remain a cause for concern because they may serve as a potential source of ongoing microbial exposure. (*PNAS* 104: 9029-9034, 2007) •

Giardia Genome Unlocked

An international team led by MBL researchers has described the complete genome of *Giardia lamblia*, one of the most common human parasites and the cause of more than 20,000 intestinal infections a year in the United States. Their findings, published in *Science*, could lead to the development of new drugs to combat this persistent infection, called giardiasis. *Giardia* lives in the human intestine in a swimming and feeding form, which is expelled through the stools. Outside the body, *Giardia* takes the form of a highly infectious cyst that can live for weeks in water, soil, food, or on other surfaces. Giardiasis is common among children, especially those in daycare facilities where it can be transmitted from children still in diapers, as well as among swimmers, hikers, campers, and travelers who drink untreated water. Analysis of the *Giardia* genome revealed several unusual proteins that are promising drug targets, according to MBL associate research scientist Hilary Morrison, first author on the paper. The MBL team also investigated the evolutionary history of *Giardia*, a single-celled eukaryote, and found its genome is compact compared to other eukaryotes, with simplified machinery for basic processes such as DNA replication and RNA processing. If the *Giardia* genome had originally been complex and experienced gene loss over evolutionary time, Morrison says, one would expect to see parts of the machinery intact and parts missing. This, however, wasn't the case. "It looks like the genome was just simpler to begin with," she says. The authors hypothesize that *Giardia* diverged from other eukaryotes more than a billion years ago. (*Science* 317: 1921-1926, 2007) •

Rising Starlet: Sea Anemone Provides Deeper Look Into Animal Evolution

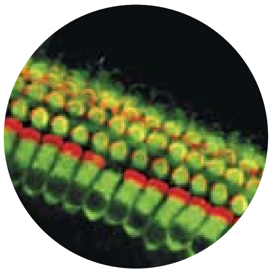
An encounter at the MBL in 2002 between a California physicist and an embryologist from Hawaii has led, five years later, to a striking, new perspective on animal evolution. In a paper published this year in *Science*, the genome of the starlet sea anemone, *Nematostella vectensis*, was analyzed by a team that included Daniel Rokhsar of the Department of Energy Joint Genome Institute (JGI), and Mark Martindale of the University of Hawaii at Manoa. The genome of this tiny invertebrate turns out to be almost as complex as that of a human being, which implies that their common animal ancestor, which lived some 700 million years ago, contained most of the genes needed to build the sophisticated organisms we find today. The starlet sea anemone was found to have about 18,000 genes, comparable to the human genome with 20,000 genes, and about two-thirds of each animal's genes are modern versions of genes that were in the shared ancestral genome. "One major lesson here is that there is no simple relationship between what we perceive as the complexity of a body plan and the number of genes," says Martindale, an instructor in the MBL's Embryology course. Why the sea anemone has kept a complex genome over the course of evolution yet has a simple body plan, while other animals have lost genes but gained physiological sophistication, opens up interesting questions. Rokhsar led the genome sequencing project with Nicholas J. Putnam of the JGI, who is an MBL Embryology course alumnus. (*Science* 317: 86-94, 2007) •

Bye, Bye Blackbird?

Overdevelopment in North America is a pressing issue, apparently even for the birds. In fact, in a *BioScience* article published this year, MBL Ecosystems Center adjunct senior scientist Ivan Valiela suggests circumstantial evidence of a link between urban sprawl and a marked decrease in the abundance of birds breeding in North America. Valiela and co-author Paulina Martinetto (Universidad Nacional de Mar del Plata) analyzed mountains of observational data collected between 1966 and 2005 by the North American Breeding Bird Survey to conclude that over the past 40 years, the total number of birds nesting in the eastern and central United States has decreased by as much as 18 percent in some areas. The losses were especially apparent among species that spend their lives within the United States and Canada, and were most pronounced among birds preferring open, edge, and wetland habitats—areas commonly impacted by industrialization and urban sprawl. The scientists also found that, contrary to what might be expected from the broadly publicized loss of tropical habitats, abundance of species that migrate to the neo-tropics or beyond did not change significantly or increased over the same time frame. Although these observations raise as many questions as they answer, the scientists point out that if human activity is indeed affecting North American birds, our ecological footprints—for better or worse—often extend well beyond the point of origin. The results provide a wake-up call for further investigations into these trends and what they mean on a global scale. (*BioScience* 57: 360-380, 2007) •

New Cell Culturing Method Pumps Up the Volume for Hearing Loss Researchers

In a breakthrough that will likely accelerate research aimed at cures for hearing loss, tinnitus, and balance problems, scientists have perfected a laboratory culturing technique that provides a new source of cells critical to understanding inner-ear disorders. A paper published in the *Proceedings of the National Academy of Sciences* by MBL Whitman investigators Zhengqing Hu and Jeffrey Corwin, both of the University of Virginia School of Medicine, described a technique for isolating cells from the inner ears of chicken embryos, growing them in the laboratory, and inducing them to form specialized receptor cells in culture. The cells, known as hair cells, are the essential sound and balance detectors of the inner ear and damage to them—from over exposure to loud sounds, adverse reactions to medications, infections, and aging—is the most common cause of significant hearing loss. Humans are born with a limited number of these cells and, until now, researchers have been hampered by difficult procedures required to gather even small numbers of these cells.



Hu and Corwin were able to freeze the cultured cells, and grow large numbers of new cells from thawed cultures—a discovery that will make hair cells accessible to more researchers and remove a significant barrier to the development of hearing loss treatments. (*PNAS* 104: 16675-16680, 2007) •

From Deep Sea to Deep Space

We live in the light, in the brilliant sphere of life that thrives on energy from the sun. But Julie Huber likes the deep, dark ocean floor, where sunlight doesn't reach. Staying alive is another story altogether, down there. And it's no stretch to imagine that the deep sea harbors the kinds of life we could find on other planets.

Vital Statistics: Julie Huber

POSITION: Assistant scientist and faculty, Josephine Bay Paul Center, MBL

DEGREES: B.S. in Marine Science, Eckerd College; M.S. and Ph.D. in Oceanography with Certificate in Astrobiology, University of Washington

YOU FIND IT, YOU NAME IT: In the Mariana Arc, Huber and others named a vent that looked like it had big hair "Marge," and others nearby "Bart" and "Homer," after the cartoon, "The Simpsons."

It's an idea that first captivated Huber when she was an undergraduate in marine science, and a meteorite from Mars rocketed into her career plans.

That was in 1996, when Huber was looking for signs of life called biosignatures in Bahamian sands, trying to figure out how the sands had formed. That year, a sensational paper in *Science* claimed to find evidence of microbial life in a Martian meteorite that had turned up in Antarctica.

"We obviously made the connection to our research," Huber says. "That's when I got excited about astrobiology. President Clinton stood in front of the White House and talked about the Martian meteorite, so it was hard not to pay attention!"

A lot of other people paid attention, too, and the meteorite sparked a surge of interest in the search for extraterrestrial life. NASA launched its Astrobiology Institute in 1998, which the MBL joined as one of ten founding team members. Huber became one of the first students to enroll in the University of Washington's Certificate in Astrobiology program while continuing her Ph.D. work in oceanography. And she started looking at "extreme environments" on Earth—places that are extraordinarily hot, acidic, radioactive or otherwise hostile to life. The hardy organisms that survive there, astrobiologists say, might thrive in similar conditions on distant planets.

"That's when I got excited about astrobiology. President Clinton stood in front of the White House and talked about the Martian meteorite, so it was hard not to pay attention!"

— Julie Huber

For her graduate work, Huber steered toward deep-sea hydrothermal vents, the super-hot, volcanic geysers that push up through the seafloor. Ever since the exciting discovery of hydrothermal vents in 1977, people had wondered if these strange environments could be where life originated on Earth, or could be found on other planets.

"This is a fundamentally different ecosystem than the photosynthetic, light-driven surface world we are familiar with," Huber says.

The huge tube worms and other odd vent creatures get all the TV coverage, but Huber is interested in the unique microbes that live in and around the vents. Many of these microbes don't need sunlight or oxygen to survive, and some can fix carbon and provide energy to all other life forms at the vent.

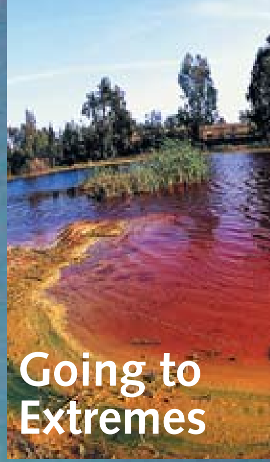
By the time Huber came to the MBL in 2005, she had spent months on research cruises to hydrothermal vent fields in the Pacific Ocean. Her data fit perfectly with the International Census of Marine Microbes then being launched at the Josephine Bay Paul Center.

"It was good timing," Huber says. "And the genomic revolution was taking over, especially in microbial oceanography, so I was looking for a place where I could really focus on genomics. The MBL was an obvious choice."

The big questions of astrobiology—"What is life? How does it originate?"—pique Huber's curiosity. She wonders whether a hydrothermal vent system could lie beneath the ice sheath that envelops Europa, Jupiter's moon, or on Mars. But what really excites Huber are the times at sea when, from a video monitor on the ship, she watches a remotely operated vehicle drop deep below the surface into a vent field.

"There is all sorts of cool science going on during these cruises," she says. "There are people studying the vent worms, the clams, the chemistry, the rocks. We are all sitting together doing science on the seafloor."

Last year, on a cruise to the Mariana Arc in the western Pacific, a deep-sea volcano erupted before their eyes. "It was like nothing anybody had seen before," Huber says. "We spent a week watching it. We had all these other tasks we wanted to do going up the Arc, but nobody wanted to leave. It was just amazing." •



Going to Extremes

Linda Amaral Zettler is an associate research scientist at the JBPC.

In searching for life beyond Earth, we are searching for the secrets to ourselves.

No doubt, finding the simplest microbes on Mars would spark tremendous excitement. But still, we would wonder. What about the microbes most like human cells, the eukaryotes? Are they out there, too, in the harsh conditions on the red planet?

That's a question for Linda Amaral Zettler of the Josephine Bay Paul Center. Amaral Zettler studies the microbes found in one of the most Mars-like places known on Earth, the Rio Tinto in southwestern Spain. This extremely acidic river is chock-full of dissolved minerals, especially iron and sulfur, which turn the river a deep-red-wine color. Mars, too, is rich in iron and sulfur, and appears to have the basic medium of life—liquid water—below its cold surface.

"What sets the Rio Tinto apart from other extreme environments on Earth is the eukaryotic diversity," Amaral Zettler says. In many hostile environments, only bacteria or archaea are to be found. But the Rio Tinto supports a rich array of eukaryotic microbes, some of which depend on the end-products of photosynthesis to survive. And that, she says, is of great interest to NASA.

Amaral Zettler's laboratory recently analyzed the bacteria found in Rio Tinto samples. Now, they're looking for archaea and eukarya, using a novel DNA sequencing strategy that can capture all three domains of microbial life in one river sample. That diversity profile will then be combined with information on the Rio Tinto's minerology, which other members of the MBL Astrobiology team are collecting. And the total picture will help NASA to interpret the remote sensing data they are receiving from Mars.

The red planet may be a world unto itself, but so in many ways is the extreme ecosystem of the Rio Tinto. "Understanding how the physical and chemical environment shape the microbial diversity we see there," says Amaral Zettler, "is key." •

Starting off with a Bang!

The MBL's Microbial Diversity Course Jumps Right In

It's dusk on a muggy, June evening at Cedar Swamp in Woods Hole. Bullfrogs boom and occasionally a fish nips at the water's black surface. The mosquitoes, it seems, would keep most humans away, but wait! Here comes a crew of young men and women, tromping down the path to the water's edge.

The two men who seem to be in charge pull out a big, plastic funnel and a butane lighter. Amid laughter, they wade into the swamp, push the funnel underwater to the mucky bottom and, after a few minutes, flick the lighter in the air above the funnel's spout. Whoosh!—a huge flame ignites, obscuring the leaders' heads and eliciting cheers from the people on shore. Then they all clamber into the swamp, pass around the funnel and try it, too.

This ritual is a clear sign that the MBL's Microbial Diversity course is back for the summer. For years, students in the course have gotten to know each other at this memorable "mixer," which also etches in their minds that microbes degrading the swamp muck release methane, a flammable gas. Former course director Ralph Wolfe of the University of Illinois at Urbana-Champaign started the swamp ritual in 1975, and it has become almost as famous as the course itself.

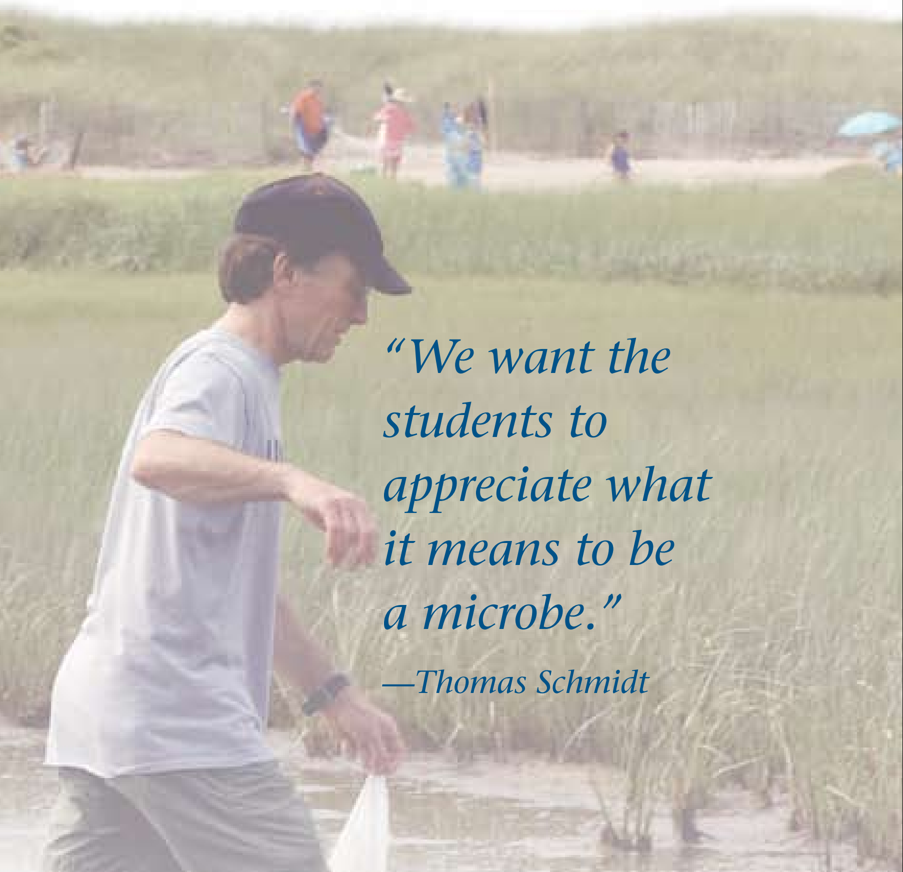
"Wow! This is really cool. I'm going to go do that," thought Dave Berry, a doctoral student at the University of Michigan, when he saw a picture of "swamped" Microbial Diversity students in the classic textbook, *Brock Biology of Microorganisms*. That photo, he says, inspired him to apply, and he attended the course last summer.

The swamp methanogens are just one of the myriad microbes that the students get to know over the intensive six-week course.

"We look at the diversity of microbes—evolutionary, ecological, and metabolic diversity—and we try to give the students a better perspective of microbial life from those three angles," says course co-director Thomas M. Schmidt of Michigan State University. "We want the students to appreciate what it means to be a microbe."

"We also want them to (understand) the role of microbes in the global environment, which is a dominant one," adds co-director William W. Metcalf of the University of Illinois at Urbana-Champaign.

The course is an immersion, with fieldwork, daily lectures, and lab studies. The students also conduct independent research projects that can take on a life of their own. "People have launched research



> *"We want the students to appreciate what it means to be a microbe."*
>
> *—Thomas Schmidt*

careers with the organisms they have isolated in this course," Schmidt says. "Articles have been published based on work begun in the course. There are real discoveries that take place." As just one example, during the 2000 course Bradley Stevenson, now at University of Oklahoma, and John Waterbury of the Woods Hole Oceanographic Institution began a project with a bacterium isolated from a Woods Hole marsh. They published their results in the April 2006 issue of *The Biological Bulletin*.

But on the first day of the course, all this lies ahead of the well-rested, eager students. Before setting out on their swamp walk, Wolfe tells them the story of Alessandro Volta, the Italian physicist who invented the battery in 1800. Volta also published the first paper on methane, which he collected by stirring the bottom sediment of a lake and bottling the gas that bubbled up. Volta didn't know what the gas was, but he experimented with it.

Wolfe holds up a homemade "pistola," the chamber Volta invented for his experiments, and then he lights the methane/air mixture inside. Most satisfactorily, it blows like a firecracker, sending the pistola's cork ricocheting off the classroom ceiling.

After the students stop cheering, Schmidt comments, "Like any good scientist, Volta wanted to see if the gas ignited!" •

Giants in Microbiology

An inspirational forefather of the MBL Microbial Diversity course was **C.B. van Niel**, who introduced one of the earliest courses in general microbiology in 1928 at Hopkins Marine Station, Stanford University. Van Niel took the broadly ecological approach to microbiology that his teachers, **M.W. Beijerinck** and **A.J. Kluyver**, had pioneered in Delft, Netherlands. Like van Niel's course, the MBL course offers a survey of the microbial world, emphasizing the diversity of microbial metabolism. Students learn how to isolate microorganisms from their natural environments—which can range from a termite's gut to a local marsh—using classical Delft enrichment techniques, in which specific conditions are set up in laboratory culture to favor the growth of the microbe of interest.

In 1954, **Ralph Wolfe** of the University of Illinois at Urbana-Champaign audited van Niel's highly regarded course and, inspired, went home and set up a similar course. When **Holger Jannasch** of the Woods Hole Oceanographic Institution called Wolfe in 1971 and invited him to teach in the new Microbial Ecology course he was starting at the MBL, Wolfe agreed. "The students showed up with nets and scuba diving equipment," Wolfe recalls, and were disconcerted to find they would be in the laboratory isolating microorganisms. Jannasch, who also admired van Niel, would become well known in the late 1970s for his work on microbiology at deep-sea hydrothermal vents. The MBL course he founded was later renamed Microbial Diversity, and it counts a "who's who of microbiology" among its alumni, says present course co-director **William Metcalf**, a colleague of Wolfe's at the University of Illinois.

The Delft lineage is just part of the story. One frequent lecturer in Microbial Diversity is **Carl Woese**, who worked down the hall from Wolfe in Illinois and who was the doctoral advisor of **Mitchell Sogin**, director of the Josephine Bay Paul Center. Woese, in 1977, introduced the concept of a molecular "Tree of Life," which classifies organisms by how they vary in a ribosomal RNA gene that each one carries. This approach led Woese to identify a whole new kingdom of microbial life, the Archaea. In the mid-1980s, **Norman Pace** at the University of Colorado used recombinant DNA technology to analyze environmental samples of microbes, which shows that less than one percent of the predicted species have been isolated using traditional culture techniques. In recent years, Sogin and Microbial Diversity co-director **Thomas Schmidt** have advanced ways to study microbes from many different environments based on ribosomal RNA gene sequences. The Microbial Diversity students learn how to do so as well, using the Keck Facility for DNA sequencing at the Josephine Bay Paul Center.

MBL Moment

...with

David "Paddy" Patterson

Senior Scientist, JBPC

*David Patterson's research interests in the diversity, evolution, and classification of microbes led him to the MBL in 2000. Formerly, he was head of the School of Biological Sciences at the University of Sydney, Australia. Patterson's team at the MBL is developing the information management system on biodiversity that underpins the Encyclopedia of Life. This system draws from two prior MBL efforts: uBio, a repository of taxonomic names and names-based services and tools developed in 2000 by David Remsen and Patrick Leary of the MBLWHOI Library and Patterson; and micro*scope, a names-based index of information on microorganisms developed by Patterson.*

The Encyclopedia of Life project is funded initially by the John D. and Catherine T. MacArthur Foundation and the Alfred P. Sloan Foundation.

As Grand as Life Itself

Once in a while, a scientific effort of truly historic dimensions captures the imagination of all involved. Such is the case with the Encyclopedia of Life (EOL), which has been called a "moon shot" for biology by its leading advocate, Harvard biologist E.O. Wilson. Over the next ten years, the Encyclopedia of Life will create a Web page for each of the 1.8 million named species on Earth. And, ideally, it will catalyze the discovery of new biodiversity, particularly in the largely undiscovered domains of microbes and insects. The MBL is a cornerstone institution in the giant EOL effort, along with Harvard University, the Smithsonian Institution, the Field Museum of Natural History, the Missouri Botanical Garden, and the Biodiversity Heritage Library. MBL director and CEO Gary Borisy is on the EOL Steering Committee and chairs its Distinguished Advisory Board. Cathy Norton, director of the MBLWHOI Library, is deputy director of the Biodiversity Heritage Library consortium, which is creating an open-access, digitized collection of natural history literature that will be available to the EOL. David Patterson, interviewed below, heads the EOL's Biodiversity Informatics Group.

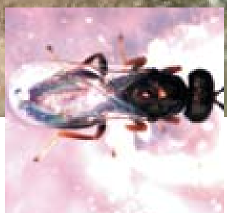
MBL By early next year, the EOL plans to have 50,000 draft pages online. This sounds ambitious! Please explain the process of creating an EOL Web page for, say, the great white shark.

DP First, the EOL is not primarily an environment where people will write pages about species. Rather, we presume that within ten years, most information about most species will be accessible through the Internet. And our task is to find all the relevant information, say, on the great white shark, draw it across the Internet, reorganize it and present it as an EOL page. For Version 1 of the EOL, we are identifying a number of data providers whose Web sites already contain everything we would want for an EOL page, and are establishing agreements with those providers. For example, upon agreement, our team should be able to draw out information on 30,000 fish species from FishBase within a matter of days. If there is no existing Web site that carries everything we want, then we have to bring information together from multiple Web sites and build up a new page. This process is referred to as aggregation or a mash-up.

MBL How do you create a species page that is appropriate for all potential users?

DP An important component of the EOL concept is it is a communally owned environment that will allow anybody to build screens and filters that will suit their needs. Say we have an EOL page on the great white shark that came out

> *"Kids, these days, are increasingly distant from the natural world and there is not much to involve them with it. With the EOL, we are developing the tools so they can go out, take pictures with their cell phones of organisms in their backyards, submit them to the EOL, and experts will help identify them."*
>
> *—David Patterson*



of FishBase, which is created for use by specialists. A teacher in Chicago looks at this and realizes it's pretty close to incomprehensible for a student audience. So the teacher may choose to rewrite it. What the teacher does is create a new page, which will be identified as being appropriate to a student audience. The students can then be directed to use that page. Like other visitors, they will have a "My EOL" function where they can set preferences for what kind of information they wish to see. A 14-year-old student will have a different view of EOL content than a molecular biologist will.

MBL So several versions of a species page are created in the EOL, rather than everybody having their hands on one version.

DP Yes. And that makes us very different from the standard wiki, such as Wikipedia, where there is the sense that there is one truth and the masses collectively will find that truth and articulate it. The EOL will have an enormous number of user groups, and we will create the tools to allow them to customize the environment to suit their needs.

MBL What value will the EOL bring to scientists?

DP Most biology at the moment is very parochial. That is, an individual or a small group collects a subset of information about one species or a small number of species. They publish the views that have emerged from their analyses. The raw data is then often hidden away and all one sees is a synthesis. And this creates "islands" of knowledge. There is one major exception to this: GenBank, a large, online, communal database of raw data where, for example, a scientist interested in the evolutionary history of a species can pick up molecular information on hundreds of other species and analyze it for similarities. Currently, there is no mechanism for doing that for any other aspect of the biology of an organism, such as information on aging or life-history strategies or ecology. Our vision for the EOL is that there will be a large communal pool of data and individuals can reach in and select the information that is relevant to their agenda, such as, "I would like all the information about the life-history strategies of butterflies." This development would have a truly transformational impact on biology. It would change biology from a parochial endeavor to something that is very grand in its power. Biologists would be able to move to considerably more global questions. They would work less as individuals and more as members of large teams with much grander agendas than they currently have.

MBL The EOL seems to hold enormous potential.

DP This project is a joy to be involved in. It's inspirational, it attracts people. One kid wrote me a letter that said, "I wrote my first book on snakes when I was 12 years old, and now I'm 16. And you need me because I will bring you 'street cred.'" And he is now our advocate for the EOL on the social networking sites. Kids, these days, are increasingly distant from the natural world and there is not much to involve them with it. With the EOL, we are developing the tools so they can go out, take pictures with their cell phones of organisms in their backyards, submit them to the EOL, and experts will help identify them. The data points will go into maps, which are then used to plot the distribution of species. So kids, and all contributors, can add to the scientific analysis of global climate change—probably the matter of greatest concern for this world. •

Gifts & Grants

- **Howard Hughes Medical Institute** awarded $4 million to support the MBL's summer educational programs and infrastructure. This amount provides funding for courses from 2008 through 2011. A grant for $725,225 was also awarded to support a pre-college science education program, The *Wolbachia* Project: Discover the Microbes Within!, developed by Seth Bordenstein of the MBL's Bay Paul Center.

- **The Ellison Medical Foundation** awarded nearly $2 million in support of the Encyclopedia of Life (EOL). The award will be used to create a comparative aging and lifespan portal within the EOL that will facilitate the identification and subsequent testing of emerging hypotheses associated with aging research.

- **The National Institutes of Health** awarded $1,104,875 for the Embryology course and $1,190,600 for logistical and technical support of the National Institute of Neurological Disorders and Stroke (NINDS) program at the MBL.

- **The National Science Foundation** awarded $820,000 in support of the Plum Island Ecosystem LTER project. The project is led by Chuck Hopkinson of the MBL's Ecosystems Center. •

Accolades

- **Jerry Melillo**, MBL senior scientist and co-director of the Ecosystems Center, has been inducted into the American Academy of Arts and Sciences. MBL Whitman investigator **Avram Hershko** (Technion-Israel Institute of Technology) was named a Foreign Honorary Member.

- **Mitchell Sogin**, MBL senior scientist and director of the Josephine Bay Paul Center for Comparative Molecular Biology and Evolution, received the American Society for Microbiology's USFCC/J. Roger Porter Award. The award recognizes Sogin for his lifetime contributions to microbial diversity and for his leading-edge work in development of an environmental microbial diversity survey.

- MBL Corporation member **Osamu Shimomura** was among six artists and scholars who received the 2007 Asahi Prize, which is awarded by the Japanese newspaper *Asahi Shimbun* "for achievement in scholarship or the arts that has made a contribution to culture or society." Shimomura was recognized for his discovery of green fluorescent protein (GFP).

- **Gerald Weissmann**, member of the MBL Corporation and Board of Trustees, is chairman of the Prix Galien USA Committee. The Prix Galien, considered the most prestigious international biomedical industry research award, is expanding its reach to the United States with this new award.

- **Douglas A. Melton**, MBL Trustee and co-director of the Harvard Stem Cell Institute, was featured as one of *Time Magazine's* 100 people "who shape our world." For more than a decade, Melton has studied how embryonic stem cells give rise to the pancreas and its insulin-producing beta cells, which are destroyed in patients with type 1 diabetes.

- MBL assistant scientist **Julie Huber** received a 2007 L'Oréal USA Fellowship for Women in Science. Huber studies how microbial populations function in and regulate the world's oceans.

- MBL Corporation member **John G. Hildebrand** (University of Arizona) was elected to membership in the National Academy of Sciences. •

On the Fast Track

As soon as MBL microbiologist Mitchell Sogin heard the buzz about the new "massively parallel" DNA sequencer invented by 454 Life Sciences, he wanted to know more.

True, the sequencing technology he already had was on par with even the largest genome centers (but at a smaller scale). The Josephine Bay Paul Center had been building a state-of-the-art sequencing facility since 2000, thanks to generous funding from the W.M. Keck Foundation.

But Sogin was facing the daunting task of identifying thousands, maybe millions, of different microbial species for the International Census of Marine Microbes. The throughput and operational cost of his current DNA sequencer just couldn't meet the challenge. And Sogin had an idea he wanted to test. Maybe the microbes in a sample of ocean could be identified by how they vary in a small region of the same gene (the V6 region of the 16s rRNA gene) rather than by sequencing the whole gene or even whole genomes.

So Sogin contacted 454 Life Sciences at their Connecticut offices and arranged to test his idea on their equipment. It worked, and amazingly well. "For the same amount of money, we can sample maybe 100 times more molecules from the environment" with the 454 than with a standard sequencer, Sogin says. He dubbed his new approach "454 tag sequencing."

Like most sequencers, the 454 provides a readout of the chemical bases that are strung in various orders along DNA strands. But the 454 cuts out the major, time-consuming step of cloning (copying) the DNA before sequencing. "That's where the really big savings come in," Sogin says.

"This is a great tool for sampling microbial diversity," says JBPC associate research scientist Hilary Morrison. "Determining microbial community composition with a traditional cloning approach can take months or even years of work. Now, we can analyze up to 32 different environmental samples in a single, five-hour run of the sequencer. It's revolutionizing how people design their studies." •

Hilary Morrison demonstrates the 454 Life Sciences sequencer in the JBPC's Keck Ecological and Evolutionary Genetics Facility, which she manages. Morrison's laboratory at the JBPC conducts research on parasite genomics and bioinformatics. Recently, a team led by Morrison finished sequencing the genome of the human parasite *Giardia lamblia*, which causes one of the most common parasitic infections in the world.

The Micro-Eco Vision

Gary G. Borisy became the MBL's thirteenth director and third CEO in 2006. He came to the MBL from Northwestern University, where he was associate vice president for biomedical research and the Leslie B. Arey Professor of Cell and Molecular Biology in the Feinberg School of Medicine. One of the cell pioneers of our time, in 1965 Dr. Borisy discovered the protein tubulin, which comprises a key part of the cell's cytoskeleton. He has also provided important insights into cell motility, chromosome movement, and cell division. Dr. Borisy is the author of more than 200 papers and the editor of two books. He has received numerous professional honors throughout his career, including an NIH MERIT Award and membership in the American Academy of Arts and Sciences. A former president of the American Society for Cell Biology, he is currently a member of the Steering Committee and Distinguished Advisory Board for the Encyclopedia of Life project (see page 12); the Board of Scientific Counselors of the National Heart Lung and Blood Institute; and the Scientific Advisory Board of the biotech company CombinatoRx.

by Gary G. Borisy

Everywhere in the sea, soil, and human body, fantastically complex communities of microbes are essential mediators of biological and chemical processes. From this intricate interplay of microbes and their environment, major issues of planetary sustainability and human health arise. Yet we still know little about the structure and function of microbial communities in nature.

As we look to the future, it's clear that the MBL is perfectly situated to invest in the nascent science of "micro-eco." Micro-eco builds on the mature science of microbial ecology, yet adds powerful, new tools for describing microbial diversity. The MBL's internationally renowned research centers—The Ecosystems Center and the Josephine Bay Paul Center—already bring tremendous resources to the analysis of microbial communities. Our goal is to leverage the strengths of these two centers to form a new, high-impact, interdisciplinary initiative at the micro-eco interface.

The Ecosystems Center is a world leader in earth systems modeling, investigating key processes such as the carbon, nitrogen, and sulfur cycles. Since all of these are mediated by microbes, microbial ecology has been a strong component of the center since 1975. The Bay Paul Center combines its strengths in molecular evolution with new strategies that employ state-of-the-art, high-throughput DNA sequencing technologies to sample the composition and relative abundance of nearly all members of microbial communities. Together, these two centers represent a confluence of expertise not found in any other institution.

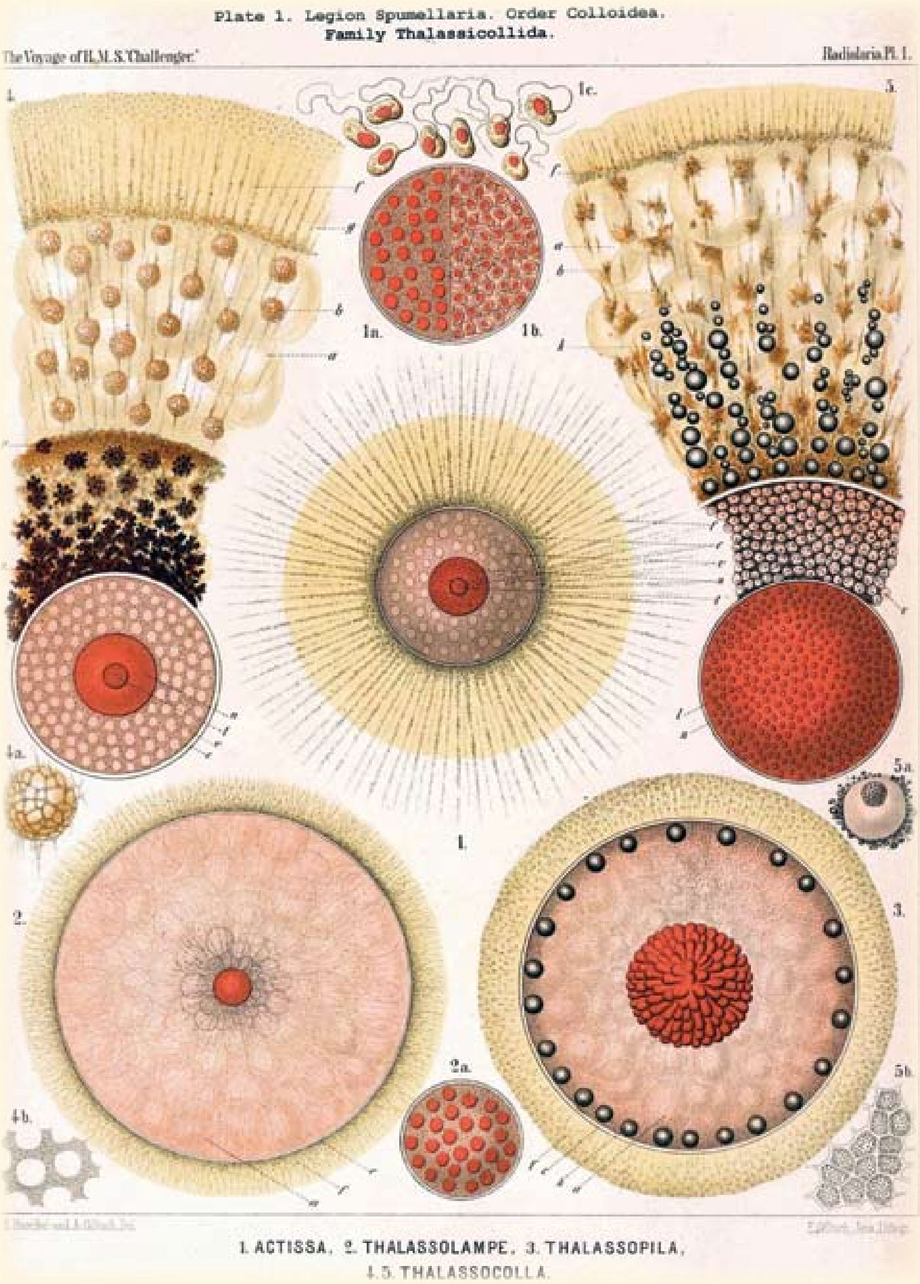
To support our investment in micro-eco, the MBL is actively recruiting leading scientists in the fields of microbial ecology and evolution, comparative genomics, and bioinformatics. We see this as a sound investment. The potential benefits to society of understanding the capabilities of microbes in nature are enormous, and they range from harnessing new sources of energy to mitigating global warming to discovering new therapeutics.

One example of micro-eco innovation at the MBL is a project to assess microbial distribution at 13 different marine and freshwater sites. Each of these is a Long-Term Ecological Research (LTER) site, and three of them are directed by Ecosystems Center scientists. The exciting challenge here is to marry molecular measures of microbial diversity with the years of baseline ecological measures being collected at the LTERs. The Bay Paul Center is populating a database, called Microbis, with genomic and environmental data and creating the software required to visualize "landscapes" of biodiversity (VAMPS: Visual Analysis of Microbial Population Structures). This kind of technology-driven, comparative, micro-eco data has never been generated before, and among those who will benefit are our LTER collaborators throughout the nation.

The biomedical opportunities at the micro-eco interface are also of great interest at the MBL. One new initiative draws on our extraordinary strengths in imaging technology. Using combinations of fluorescent probes, we will actually see how tens to hundreds of different kinds of microbes are spatially arranged—be they in a seawater sample or in the human mouth. New "starlight" spectral imaging technology could have broad diagnostic applications, both in medicine and in environmental management.

Microbes are the unseen majority. Making the connection between microbes and our environment is first-rate science at the MBL, and of first-rate importance to society. •

TREASURES FROM THE MBL'S RARE BOOKS ROOM



From *Report on the Scientific Results of the Voyage of the H.M.S. Challenger During the Years 1873-1876, Zoology, Volume XVIII: Report on the Radiolaria*, by Ernst Haeckel, M.D., Ph.D., Professor of Zoology, University of Jena, published 1887. The 50-volume set of the *H.M.S. Challenger* biological reports is in the Special Collections of the MBLWHOI Library.

Nature is Greatest in the Smallest Things

Ernst Haeckel was one of the most famous, if controversial, biologists of the 19th century. Although at times he took artistic license with his beautiful scientific illustrations, Haeckel's monograph on the Radiolaria, a class of microscopic protozoans, is considered one of his lasting and factual contributions to biology. Thinking the work would take a few years, in 1876 Haeckel accepted the "enticing invitation" to report on the Radiolaria species that had been collected during the just-completed voyage of the *H.M.S. Challenger*. This voyage, which is often called the birth of oceanography, covered nearly 69,000 nautical miles and took both shallow and deep-water samples at 362 stations. As it turned out, Haeckel's Radiolaria study took a full ten years. "The further my investigations proceeded, the more immeasurable seemed the range of forms, like the boundless firmament of stars," he wrote. Haeckel described 3,508 new species of Radiolaria in the *Challenger* report, yet noted "for a really complete examination, the lifetime of one man would not suffice." He hoped his devoted effort would inspire naturalists "to study more deeply this inexhaustible kingdom of microscopic life, whose endless variety of wonderful forms justifies the saying, *'Natura in minimus maxima.'*" •

In the Next *Catalyst*

Learning to Love Science The MBL's widely influential, graduate-level summer courses have gained a worldwide reputation since the first one was launched in 1888. Today, the exciting summer season at the MBL extends well into the spring and fall with courses for postgraduates, undergraduates, science teachers, historians, and science writers. And the joint MBL-Brown University Ph.D. Program in Biological and Environmental Sciences keeps the campus humming year-round. In the next issue of *MBL Catalyst*, meet some of the visionary teachers and students who make the MBL a beacon of biological training.

MBL Biological Discovery in Woods Hole

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